4165-15-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

42 CFR Part 110

RIN 0906-AB22

Countermeasures Injury Compensation Program: Smallpox Countermeasures Injury Table

AGENCY: Health Resources and Services Administration (HRSA), Department of Health and Human Services (HHS).

ACTION: Final rule.

SUMMARY: HHS is establishing the Smallpox Countermeasures Injury Table (Table) as authorized by the Public Readiness and Emergency Preparedness Act of 2005 (PREP Act). Through this final rule, the Secretary of the U.S. Department of Health and Human Services (Secretary) adds the Smallpox Countermeasures Injury Table to the agency's regulations. The Table includes a list of covered smallpox countermeasures, required time intervals for the first symptom or manifestation of onset of injuries, and the accompanying Qualifications and Aids to Interpretation (QAI), which set forth definitions and other requirements necessary to establish Table injuries.

DATES: This rule is effective **[INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]**.

FOR FURTHER INFORMATION CONTACT: Tamara Overby, Acting Director, Division of Injury Compensation Programs, Healthcare Systems Bureau, HRSA, 5600 Fishers Lane, 8N146B, Rockville, MD 20857, or by telephone (855) 266-2427. This is a toll-free number.

SUPPLEMENTARY INFORMATION: On October 15, 2020, HHS published a notice of proposed rulemaking (NPRM) in the **Federal Register** (85 FR 65311) proposing to add the Table for designated covered smallpox countermeasures identified in the Smallpox Medical Countermeasures PREP Act declaration. The Table includes a list of smallpox countermeasures,

proposed time intervals for the first symptom or manifestation of onset of injury, and Qualifications and Aids to Interpretation which set forth the definitions and requirements necessary to establish the Table injuries. The NPRM provided a 60-day comment period, and HHS received one out-of-scope comment.

I. Background and Purpose

The PREP Act authorizes the Countermeasures Injury Compensation Program (CICP) to provide compensation to certain individuals who develop serious physical injuries or to certain survivors of individuals who die as a direct result of the administration or use of a covered countermeasure identified in a PREP Act declaration.[1] In carrying out the CICP, the PREP Act directs the Secretary to establish, through regulation, a Covered Countermeasures Injury Table (Table) identifying serious physical injuries that are presumed to be directly caused by the administration or use of covered countermeasures identified in PREP Act declarations issued by the Secretary. The Secretary may only add to a Table injuries that are directly caused by the administration or use of the covered countermeasure based on "compelling, reliable, valid, medical and scientific evidence."[2] The Table informs the public about serious physical injuries known to be directly caused by covered countermeasures and creates a rebuttable presumption of causation for eligible individuals whose injuries are listed on the Table and meet the Table's requirements.

The CICP's regulations, which detail the Program's requirements, are found at 42 CFR part 110. The provision at 42 CFR 110.20(a) states that individuals must establish that a covered injury occurred to be eligible for benefits under the Program. A covered injury is death or a serious injury determined by the Secretary to be: (1) an injury meeting the requirements of a Table, which is presumed to be the direct result of the administration or use of a covered

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[1] *See* Department of Defense, Emergency Supplemental Appropriations to Address Hurricanes in the Gulf of Mexico, and Pandemic Influenza Act of 2006, Part C (Pub. L. 109-148); 42 U.S.C. 247d-6e.

[2] 42 U.S.C. 247d-6e (b)(5)(A).

countermeasure unless the Secretary determines there is another more likely cause; or (2) an injury (or its health complications) that is the direct result of the administration or use of a covered countermeasure.[3] This includes a covered countermeasure causing a serious aggravation of a pre-existing condition.[4] In general, only injuries that warranted hospitalization (whether or not the person was actually hospitalized), or injuries that led to a significant loss of function or disability are considered serious injuries.[5]

Individuals with injuries not meeting the requirements of the Table may still pursue their claims as non-Table injuries under the Program.[6] In that instance, the requester does not receive the presumption of causation for a Table injury and must demonstrate that the administration or use of the covered countermeasure directly caused the injury.[7] Proof of a causal association for the non-Table injury must be based on compelling, reliable, valid, medical and scientific evidence.[8]

II. Summary of the Final Rule

Through this final rule, the Secretary adds the Smallpox Countermeasures Injury Table to subpart K of 42 CFR part 110. The Table established in this final rule is limited to smallpox covered countermeasures identified in the Secretary's PREP Act Declaration for Smallpox Medical Countermeasures.[9]

The Smallpox Countermeasures Injury Table lists several smallpox covered countermeasures and serious physical injuries that, based on compelling, reliable, valid, medical and scientific evidence, are directly caused by the administration or use of the associated covered countermeasures. The Table provides the serious injuries associated with a specific countermeasure and the time interval within which the first symptom or manifestation of onset of

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[3] 42 CFR 110.3(g).
[4] *Id*.
[5] 42 CFR 110.3(z).
[6] 42 CFR 110.20(c).
[7] *Id.*
[8] *Id.*
[9] 80 FR 76546 (Dec. 9, 2015).

injury must appear. The QAI, which accompany the Table, are definitions included to further explain the requirements for each covered injury and the level of severity necessary to qualify as a Table injury. The Secretary will stay informed of updates in the scientific and medical field concerning potential new information about causal associations between injuries and covered countermeasures and update the Table as needed.

In accordance with 42 CFR 110.42(f), in addition to the standard filing deadline, with the publication of this new Table, certain eligible requesters have one year from the effective date of the publication of the Table to file claims for injuries that meet the Table's requirements. Individuals who sustained injuries that are not included on the Table or that do not meet all of the requirements for a Table injury, but who may prove causation of the injury through other means, are not eligible for the additional one-year filing deadline based on the Table's publication. Because the new Table would not enable such individuals to establish a Table injury, they would be subject to the standard filing deadline in 42 CFR 100.42(a) (i.e., one year from the date of administration or use of the covered countermeasure).

In this final rule, the Secretary has made the following change from what was proposed in the NPRM for the purposes of clarity.

a. Changed paragraph (d)(6) by adding a comma after "pustules)" and before "generally" to the second sentence. The revised sentence states, "The rash or lesions, characterized by multiple blisters (vesicles or pustules), generally evolve in a similar sequence or manner as the original vaccination site.
b. Changed paragraph (d)(9) by adding "to" after "attributed" and before "it" to the seventh sentence. The revised sentence states, "Symptoms that occur before 5 days or more than 14 days after receiving the smallpox vaccine should not be attributed to it."

III. Comments and Responses

The NPRM set forth a 60-day public comment period, which ended on December 14, 2020. During the comment period, HHS received one comment that was not relevant to the NPRM. As noted above, the only changes made to the final rule are to paragraphs (d)(6) and (9) for clarity.

IV. Regulatory Impact Analysis

HHS examined the impact of this final rule as required by Executive Order 12866 on Regulatory Planning and Review (September 30, 1993), Executive Order 13563 on Improving Regulation and Regulatory Review (January 18, 2011), the Congressional Review Act (5 U.S.C. 804(2)), the Regulatory Flexibility Act (RFA) (September 19, 1980, Pub. L. 96–354), section 202 of the Unfunded Mandates Reform Act of 1995 (March 2, 1995; Pub. L. 104–4), section 654(c) of the Treasury and General Government Appropriations Act of 1999, and Executive Order 13132 on Federalism (August 4, 1999)

Executive Orders 12866 and 13563

Executive Order 12866 requires all regulations reflect consideration of alternatives, costs, benefits, incentives, equity, and available information. Regulations must meet certain standards, such as avoiding an unnecessary burden. Regulations that are "significant" because of cost, adverse effects on the economy, inconsistency with other agency actions, effects on the budget, or novel legal or policy issues, require special analysis. In 2011, President Obama supplemented and reaffirmed Executive Order 12866.

Executive Order 13563 provides that, to the extent feasible and permitted by law, the public must be given a meaningful opportunity to comment on any proposed regulations, with at least a 60-day comment period. In addition, to the extent feasible and permitted by law, agencies must provide timely online access to both proposed and final rules of the rulemaking docket on https://www.regulations.gov/, including relevant scientific and technical findings, in an open format that can be searched and downloaded. Federal agencies must consider approaches to maintain the freedom of choice and flexibility, including disclosure of relevant information to the

public. Objective scientific evidence guides regulations and should be easy to understand, consistent, and written in plain language. Furthermore, Federal agencies must attempt to coordinate, simplify, and harmonize regulations to reduce costs and promote certainty for the public.

Summary of Impacts

In this final rule, the Secretary establishes a Table identifying serious physical injuries that are presumed to result from the administration or use of certain covered countermeasures, required definitions of those injuries, and the time interval in which the onset of the first symptom or manifestation of each injury must manifest for the presumption of causation to apply. The Table establishes a presumption of causation for requesters meeting the Table's requirements and relieves requesters of the burden of demonstrating causation. However, this presumption is rebuttable if, based on the Secretary's review of the evidence, a source other than the countermeasure is found to be the more likely cause of the injury. The publication of this Table may afford some requesters a new filing deadline.

The Secretary has determined that minimal staff and funding resources are required to implement the provisions included in this final rule. Therefore, in accordance with the Regulatory Flexibility Act of 1980 (RFA) and the Small Business Regulatory Enforcement Fairness Act of 1996, which amended the RFA, the Secretary certifies that this final rule will not have a significant impact on a substantial number of small entities.

The Secretary has determined that this final rule does not meet the criteria for an "economically significant" regulatory action as defined by Executive Order 12866 and would have no major effect on the economy or Federal expenditures. The Secretary also has determined that this final rule is not a "major rule" within the meaning of the statute providing for Congressional Review of Agency Rulemaking, 5 U.S.C. 801. The Office of Information and Regulatory Affairs within the Office of Management and Budget has determined that this rule is not a "significant regulatory action" within the meaning of section 3(f) of the Executive order.

Unfunded Mandates Reform Act of 1995

The Unfunded Mandates Reform Act of 1995 (section 202(a)) requires us to prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing "any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year." The current threshold after adjustment for inflation is $158 million, using the most current (2020) Implicit Price Deflator for the Gross Domestic Product. This final rule would not result in an expenditure in any year that meets or exceeds this amount.

Executive Order 13132—Federalism

The Secretary also reviewed this final rule in accordance with Executive Order 13132 regarding federalism and has determined that it does not have "federalism implications." This final rule will not "have substantial direct effects on the states, or on the relationship between the national government and the states, or on the distribution of power and responsibilities among the various levels of government."

Paperwork Reduction Act of 1995

This final rule has no information collection requirements.

List of Subjects in 42 CFR Part 110

Biologics, Immunization.

Dated: August 9, 2021.

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Xavier Becerra,

Secretary,

Department of Health and Human Services.

PART 110—COUNTERMEASURES INJURY COMPENSATION PROGRAM

1. The authority citation for part 110 continues to read as follows:

Authority: 42 U.S.C. 247d–6e.

2. Amend § 110.100 by revising paragraph (b) introductory text and paragraph (c) and adding paragraph (d) to read as follows:

§110.100 Injury Tables.

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(b) *Qualifications and aids to interpretation (table definitions and requirements).* The following definitions and requirements shall apply to the Table set forth in paragraph (a) of this section and only apply for purposes of this subpart.

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(c) *Smallpox countermeasures injury table.*

Table 2 to Paragraph (c)

Covered Countermeasures under Declarations	Serious Physical Injury (illness, disability, injury, or condition)[1]	Time Interval (for first symptom or manifestation of onset of injury after administration or use of covered countermeasure, unless otherwise specified)
I. Smallpox Vaccines Replication-Deficient	A. Anaphylaxis	A. 0-4 hours.
	B. Vasovagal Syncope	B. 0-1 hour.
II. Smallpox Vaccines Replication-Competent	A. Anaphylaxis	A. 0-4 hours.
	B. Vasovagal Syncope	B. 0-1 hour.
	C. Significant Local Skin Reaction	C. 1-21 days.

	D. Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis	D. 4-28 days.
	E. Inadvertent Autoinoculation	E. 1-21 days.
	F. Generalized *Vaccinia*	F. 6-9 days.
	G. Eczema *Vaccinatum*	G. 3-21 days.
	H. Progressive *Vaccinia*	H. 3-21 days.
	I. Post-*vaccinial* Encephalopathy, Encephalitis or Encephalomyelitis (PVEM)	I. 5-14 days.
	J. *Vaccinial* Myocarditis, Pericarditis, or Myopericarditis (MP)	J. 0-21 days.
III. *Vaccinia* Immunoglobulin Intravenous (VIGIV)	A. Anaphylaxis	A. 0-4 hours.
	B. Transfusion-Related Acute Lung Injury (TRALI)	B. 0-72 hours.
	C. Acute Renal Failure (ARF)	C. 0-10 days.
	D. Drug-Induced Aseptic Meningitis (DIAM)	D. Within 48 hours after the first dose and up to 48 hours after the last dose of VIGIV.
	E. Hemolysis	E. 12 hours to 14 days.
IV. Cidofovir	A. No Condition Covered[2]	A. Not Applicable.
V. Tecovirimat	A. No Condition Covered[2]	A. Not Applicable.

VI. Brincidofovir	A. No Condition Covered[2]	A. Not Applicable.
VII. Smallpox Infection Diagnostic Testing Devices	A. No Condition Covered[2]	A. Not Applicable.

[1]Serious physical injury as defined in § 110.3(z). Only injuries that warranted hospitalization (whether or not the person was actually hospitalized) or injuries that led to a significant loss of function or disability will be considered serious physical injuries.

[2] The use of "No condition covered" in this Table 2 reflects that the Secretary evaluated the countermeasure, but at this time does not find compelling, reliable, valid, medical, and scientific evidence to support that any serious injury is presumed to be caused by the associated covered countermeasure. For injuries alleged to be due to covered countermeasures for which there is no associated Table 2 injury, requesters must demonstrate that the injury occurred as the direct result of the administration or use of the covered countermeasure. *See* § 110.20(b) and (c).

(d) *Qualifications and aids to interpretation (table definitions and requirements).* The following definitions and requirements shall apply to the Table set forth in paragraph (c) of this section and only apply for purposes of this subpart.

(1) *Anaphylaxis*. Anaphylaxis is an acute, severe, and potentially lethal systemic reaction that occurs as a single discrete event with simultaneous involvement of two or more organ systems. Most cases resolve without *sequelae*. Signs and symptoms begin within minutes to a few hours after exposure. Death, if it occurs, usually results from airway obstruction caused by laryngeal edema or bronchospasm and may be associated with cardiovascular collapse. Other significant clinical signs and symptoms may include the following: cyanosis, hypotension, bradycardia, tachycardia, arrhythmia, edema of the pharynx and/or trachea and/or larynx with stridor and dyspnea. There are no specific pathological findings to confirm a diagnosis of anaphylaxis.

(2) *Vasovagal syncope.* Vasovagal syncope (also sometimes called neurocardiogenic syncope) means loss of consciousness (fainting) and loss of postural tone caused by a transient decrease in blood flow to the brain occurring after the administration of an injected countermeasure. Vasovagal syncope is usually a benign condition, but may result in falling

and injury with significant *sequelae*. Vasovagal syncope may be preceded by symptoms, such as nausea, lightheadedness, diaphoresis (sweating), and/or pallor. Vasovagal syncope may be associated with transient seizure-like activity, but recovery of orientation and consciousness generally occurs simultaneously. Loss of consciousness resulting from the following conditions will not be considered vasovagal syncope: organic heart disease, cardiac arrhythmias, transient ischemic attacks, hyperventilation, metabolic conditions, neurological conditions, psychiatric conditions, seizures, trauma, and situational as can occur with urination, defecation, or cough. This list is not complete as other conditions that are not associated with the vaccine also may cause loss of consciousness. Episodes of recurrent syncope occurring after the applicable timeframe are not considered to be *sequelae* of an episode of syncope meeting the Table 2 requirements.

(3) *Significant local skin reaction.* Significant local skin reaction is an unexpected and extreme response at the vaccination or inoculation site that results in a significant scar that is serious enough to require surgical intervention. The onset of this injury is the initial skin lesion at the vaccination site that generally occurs with replication-competent smallpox vaccinations. Minor scarring or minor local reactions do not constitute a Table 2 injury. A robust take, defined as an area of redness at the vaccination site that exceeds 7.5 cm in diameter with associated swelling, warmth and pain, is generally considered an expected response to the vaccination or inoculation. A robust take, in itself, does not constitute a Table 2 injury, even when the redness and swelling involves the entire upper arm with associated enlargement and tenderness of the glands (lymph nodes) in the underarm (axilla).

(4) *Stevens-Johnson syndrome/Toxic epidermal necrolysis (SJS/TEN)*. SJS/TEN is a spectrum of acute hypersensitivity reactions that affects skin, mucous membranes, and sometimes, internal organs (systemic toxicity) associated with the use or administration of replication-competent smallpox vaccines. For purposes of Table 2, both skin and mucous membrane rash or lesions must be present. Rash or lesion distribution must be widespread. Rash must

not have a symmetric acral distribution (affecting arms, hands, legs or feet). Two or more mucosal sites must be involved. Mucosal lesions generally manifest as painful lesions in sites, such as the mouth or eyes. Skin rash or lesions in SJS/TEN usually consist of red or purple raised areas (erythematous macules), blisters, and ulcerations.

(5) *Inadvertent autoinoculation (IA)*. IA is the spread of *vaccinia* virus from an existing vaccination site to a second location usually by scratching the vaccination site and subsequently spreading the virus, which produces a new *vaccinial* lesion on the same person who received the vaccination. IA is the most common adverse event associated with the replication-competent smallpox vaccine.

(6) *Generalized vaccinia (GV)*. GV is a *vaccinial* infection that occurs from the spread of *vaccinia* from an existing vaccination or inoculation site, with the use or administration of a replication-competent smallpox vaccine, to otherwise normal skin, resulting in multiple new areas of *vaccinial* rash or lesions. The *vaccinia* is believed to be spread through the blood. The rash or lesions, characterized by multiple blisters (vesicles or pustules), generally evolve in a similar sequence or manner as the original vaccination site.

(7) *Eczema vaccinatum (EV)*. EV is the transmission or the spread of *vaccinia* virus from a vaccination site, after the use or administration of a replication-competent smallpox vaccine, to skin that has been affected by, or is currently affected with, eczema or atopic dermatitis. EV is characterized by lesions that include multiple blisters (vesicles or pustules), which generally evolve in a similar sequence or manner as the original vaccination site. The lesions may come together to form larger lesions. Lesions may also spread to patches of skin that have never been involved with eczema or atopic dermatitis. The new lesions, if cultured, will be positive for *vaccinia* virus. A person with EV may become severely ill with signs and symptoms that involve the whole body (systemic illness), such as fever, malaise, or enlarged glands (lymph nodes).

(8) *Progressive vaccinia (PV).* PV is the failure to initiate the healing process in an initial vaccination or inoculation site, after the use or administration of a replication-competent smallpox vaccine, by 21 days after exposure to *vaccinia,* with progressive ulceration or necrosis at the vaccination site leading to a large destructive ulcer. PV is seen in people who are immunocompromised (have an impaired immune system) and is characterized by a complete or near complete lack of inflammation or absence of inflammatory cells in the dermis of the skin at the vaccination site. The diagnosis of PV may be made before 21 days after exposure, especially in a known immunocompromised individual who develops a lesion at the vaccination site. PV may spread through the blood to any location in the body. No one who experiences a significant healing process of the vaccination site within 21 days after receipt of the replication-competent smallpox vaccine or exposure to *vaccinia* has PV.

(9) *Post-vaccinial encephalopathy, encephalitis, and encephalomyelitis (PVEM).* PVEM is a spectrum of overlapping conditions that includes post-*vaccinial* encephalopathy, encephalitis, and encephalomyelitis, and, for the purposes of Table 2, is treated as one injury. For the purposes of Table 2, PVEM is an autoimmune central nervous system injury that occurs after the use or administration of a replication-competent smallpox vaccine. In rare cases, the *vaccinia* virus is isolated from the central nervous system. Manifestations usually occur abruptly and may include fever, vomiting, loss of appetite (anorexia), headache, general malaise, impaired consciousness, confusion, disorientation, delirium, drowsiness, seizures, language difficulties (aphasia), coma, muscular incoordination (ataxia), urinary incontinence, urinary retention, and clinical signs consistent with inflammation of the spinal cord (myelitis), such as paralysis or meningismus (meningeal irritation). Long-term central nervous system impairments, such as paralysis, seizure disorders, or developmental delays are known to occur as *sequelae* of the acute PVEM. No clinical criteria, radiographic findings, or laboratory tests are specific for the diagnosis of PVEM. Symptoms that occur before 5 days or more than 14 days after receiving the smallpox vaccine should not be

attributed to it. In addition, encephalopathy caused by an infection, a toxin, a metabolic disturbance, a structural lesion, a genetic disorder, or trauma would not meet the Table 2 definition.

(10) *Vaccinial myocarditis, pericarditis, or myopericarditis (MP).* For purposes of Table 2, MP is *vaccinial* myocarditis, pericarditis, or myopericarditis. *Vaccinial* myocarditis is defined as an inflammation of the heart muscle (myocardium) because of receiving the replication-competent smallpox vaccine. *Vaccinial* pericarditis is defined as an inflammation of the covering of the heart (pericardium) because of receiving the smallpox vaccine. *Vaccinial* myopericarditis is defined as an inflammation of both the heart muscle and its covering because of receiving the smallpox vaccine. The inflammation associated with MP may range in severity from very mild (subclinical) to life threatening. In many mild cases, myocarditis is diagnosed solely by transient electrocardiographic (EKG) abnormalities (*e.g.*, ST segment and T wave changes), increased cardiac enzymes, or mild echocardiographic abnormalities. Arrhythmias, abnormal heart sounds, heart failure, and death may occur in more severe cases. Pericarditis generally manifests with chest pain, abnormal heart sounds (pericardial friction rub), EKG abnormalities (*e.g.*, ST segment and T wave changes), and/or increased fluid accumulation around the heart. A Table 2 injury of MP requires sufficient evidence in the medical records of the occurrence of acute MP.

(11) *Transfusion-related acute lung injury (TRALI).* TRALI is defined as the onset of respiratory distress within 6 hours in non-critically ill patients, and 72 hours in critically ill patients, after receipt of blood products containing plasma, in this case, VIGIV. The relative level of illness will be determined on a case-by-case basis after reviewing the medical records and the medical history. The respiratory distress is the result of receiving a plasma containing transfusion (VIGIV) and subsequently developing pulmonary edema, respiratory distress, and hypoxia. TRALI occurs as the result of an antibody response in the host to the donor antibodies within the plasma product. Pulmonary edema is non-cardiac in nature and

does not occur more than 72 hours after receiving VIGIV. Pulmonary edema occurring more than 72 hours after receiving a blood product containing plasma (VIGIV) or associated with cardiac dysfunction is not TRALI and is excluded as a countermeasure-related injury. TRALI has been identified as a major cause of mortality in those individual receiving plasma-containing transfusions. A Table 2 injury for TRALI has occurred in a recipient if there is sufficient evidence in the medical record of an occurrence of TRALI and the pulmonary edema is not caused by cardiac dysfunction or other causes and occurs within 72 of receiving a blood product containing plasma, in this case VIGIV.

(12) *Acute renal failure (ARF).* ARF is the sudden loss of the kidneys' ability to perform their main function of eliminating excess fluids and electrolytes (salts), as well as waste material from the blood. ARF, which is also called acute kidney injury, develops rapidly over a few hours or a few days. ARF can be fatal and requires intensive treatment; however, ARF may be reversible. ARF may cause permanent loss of kidney function, or end-stage renal disease necessitating dialysis or transplant. A Table 2 injury for ARF has occurred if there is sufficient evidence in the medical record of an occurrence of ARF within the identified timeframe and the individual received the associated countermeasure (VIGIV).

(13) *Drug-induced aseptic meningitis (DIAM).* (i) DIAM is an inflammation of the meninges (linings of the brain) that is not caused by a bacteria or virus, but is caused by a drug or medication. The symptoms of meningitis include severe headache, nuchal (neck) rigidity, drowsiness, fever, photophobia (light sensitivity), painful eye movements, nausea, and vomiting. Discontinuation of the medication leads to a resolution of the symptoms. DIAM is thought to occur because of an immunological hypersensitivity reaction to a specific medication. In the case of immunoglobulins, DIAM may be precipitated by the immunologically active components within the plasma or because of the stabilizers used within the product. The symptoms of DIAM may reoccur with another exposure to the offending agent.

(ii) A Table 2 injury for DIAM has occurred in a recipient if there is sufficient evidence in the medical record of an occurrence of DIAM within the identified timeframe and the individual received the associated countermeasure (VIGIV). DIAM occurring in the absence of the use of VIGIV, or DIAM occurring with the use of VIGIV outside the established timeframe of onset, which is any time after the first dose and up to 48 hours after the last dose of this medication, is not a Table 2 injury.

(14) *Hemolysis.* Hemolysis is the physical breakdown of red blood cells (RBCs) either through natural attrition or as caused by external factors. The RBC's function is to transport oxygen throughout the body in the hemoglobin contained within the RBC. Additionally, the RBCs contain the majority of the body's potassium stores. With hemolysis, the body is unable to transport oxygen effectively, and the person develops hypoxia. Additionally, the rapid breakdown of the cell releases large amounts of potassium into the blood stream, which can cause abnormal heart rhythms and cardiac arrest. In severe cases of hemolysis, a blood transfusion may be required to correct the resulting anemia. A Table 2 injury for hemolysis has occurred if there is sufficient evidence in the medical record of an occurrence of hemolysis, and the patient received the associated countermeasure (VIGIV). Hemolysis occurring in the absence of the use of VIGIV and outside of the timeframe of 12 hours to 14 days after receiving VIGIV is not a Table 2 injury. Hemolysis occurring from a more likely alternative diagnosis, such as infections, toxins, poisons, hemodialysis, or medications, is not a Table 2 injury. This list of conditions that can cause hemolysis, not associated with VIGIV, is not exhaustive, and all additional diagnoses within the medical documentation will be evaluated.

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